Professor Cassandra Szoeke, PhD FRACP MBBS BSc(Hons) Genetics
Consultant Neurologist
Australian Commonwealth Science and Industry Research Organisation
National Ageing Research Institute
3 year follow-up almost complete – currently in data entry phase

- 25% of MCI progressed to AD
- Large shifts between NMC and SMC
- 25% AD, 23% MCI, 8% HC Lost

87% retention

114 Non-returners
28 Deceased

Baseline cohort
- 372 NMC
- 395 SMC
- 133 MCI
- 211 AD

18 MONTHS
- 317 NMC
- 374 SMC
- 81 MCI
- 196 AD

220 97 114 253 4 14 1 3 7 63 33 159

968
Organizational Structure of AIBL

Addressing population aging and Alzheimer’s disease through the Australian Imaging Biomarkers and Lifestyle study: Collaboration with the Alzheimer’s Disease Neuroimaging Initiative

Kathryn A. Ellis\textsuperscript{a,b,c,*}, Christopher C. Rowe\textsuperscript{d}, Victor L. Villemagne\textsuperscript{b,d}, Ralph N. Martins\textsuperscript{e}, Colin L. Masters\textsuperscript{b}, Olivier Salvado\textsuperscript{f,g}, Cassandra Szoke\textsuperscript{g}, David Ames\textsuperscript{a,c}; and

Management committee
D. Ames (Chair, study leader), L. Bevege, K. Ellis (study manager)
R. Martins, C. Masters, A. Milner, C. Rowe, P. Stasinos, C. Szoke

Neuroimaging stream
C. Rowe (Chair), V. Villemagne, O. Salvado, N. Lenzo

Clinical and cognitive stream
K. Ellis (Chair), P. Maruff, G. Savage

Biomarkers stream
C. Masters, R. Martins (Joint Chairs), A. Bush, B. Wilson

Lifestyle stream
R. Martins (Chair), C. Szoke
Study Databases

Clinical Cognitive

Biomarkers

Genomic

Lifestyle Intervention

Imaging

PET-PiB
Amyloid beta load

T1W
Anatomy

T2W
CSF and structures

SWI
Venous tree

FLAIR
White matter lesions

DWI
White matter connection
Organisational Structure continued

Science and Industry Endowment Fund

Science and Management Committee

Expression Of Interest

Business Development Advisory Committee

www.aibl.csiro.com.au
Early Detection
Early Detection
Early Detection
Clinical – EARLY DETECTION
– need for new norms?

• Strict Criteria for HEALTHY CONTROLS

• HC plus

  1. 11C-PiB Standard Update Value Ratio (SUVR) < 1.3
  2. No focal 11C-PiB on visual inspection
  3. Baseline MMSE > 28
  4. Clinical Dementia Rating (CDR) & CDR sum of boxes = 0
  5. Normal MRI (no hippocampal nor global GM atrophy)
  6. Geriatric Depression score < 4
  7. Cardiovascular risk factor score (CVRF) < 4
  8. Lab work with no anaemia, no liver or kidney disease, no hypothyroidism, no B12 or folate deficiency
  9. Change on MMSE at 18 month < 2
  10. No conversion from HC status at 18 month follow-up

• A significantly greater proportion of the HC and MCI AIBL groups fell 1.5 SD below the mean when compared to the sHC than when compared to the published norms

See POSTER Ellis, Rowe et al, Sunday 17th July, 1230-1500

COMMERCIAL IN CONFIDENTIALITY – CONTAINS PILOT AND UNPUBLISHED DATA
Clinical – EARLY DETECTION

• AT RISK HEALTHY GROUP

• Of the 704 “healthy controls (HC)

• 59% performed significantly better on 4 tests than the other 41%

• Those in the other 41% had a risk for conversion from HC to MCI or dementia

OR 9.72 (CI: 3.05-30.98)
Clinical – EARLY DETECTION

HC - Truly HC?

Of the 20 converters 17 were in the lower performing group
## Comparison Conversion Rates per 18 months

<table>
<thead>
<tr>
<th></th>
<th>HC-MCI</th>
<th>HC-AD</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>AIBL</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>“Better performers”</td>
<td>0.5 %</td>
<td>0.3 %</td>
</tr>
<tr>
<td>“other HC”</td>
<td>5.6%</td>
<td>1.2%</td>
</tr>
<tr>
<td><strong>ADNI</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>1.4-7.2%</td>
<td></td>
</tr>
<tr>
<td><strong>Population</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>1.5-9%</td>
<td>0.25-5.2%</td>
</tr>
<tr>
<td><strong>Memory Clinic</strong></td>
<td></td>
<td>15%</td>
</tr>
</tbody>
</table>

HC-MCI; 1-6% per annum.
HC-AD; age dependent; Fratigioni et al found 1.7 to 35.3 per 1000 person years
Clinical – EARLY DETECTION

• NOT BEING IN THE HIGHER FUNCTIONING GROUP

• 10 times the risk of conversion to MCI or dementia

Developing topics presentation

Szoeke et al., Wednesday 20th July 1600
Biomarkers– EARLY DETECTION

• Change in Biomarker levels over 18 months to predict AD
  • Creatinine
  • Neutrophils
  • High Density Lipoprotein
  • Red Cell Folate
  • Total Protein
  • Transferrin

• Low change in HC
• Higher change in AD and those who transitioned towards AD
• Sensitivity and Specificity 88%
  • adjusting for age and APOE genotype.

See poster Doecke, Faux et al 2011, Sunday 17th July, 1230-1500
AIBL: The Next 3 Years

**Clinical**
- Complete 3 and then 4.5 year follow-up

**Enrich**
- Add 200 new subjective memory complainers and MCI

**Enrich + midlife risk**
- Add 200 women from a cohort previously assessed in 2002 and 2004

**Imaging**
- Amyloid and MRI imaging in all participants, including enriched and intervention cohorts

**Lifestyle Intervention**
- “AIBL Active” – exercise intervention in 150 HC/MCI
AIBL: ongoing

- Complete 3 year follow-up by September
- Commence 4.5 year follow-up by September
- Complete recruitment of 200 new subjective memory complainers and MCI

- Funding strategy for 6 and 7.5 year follow-up
• CSF Ab42 reduction correlating with memory in female healthy elderly but not in males

• Amyloid load on Pib scans relating to cognition in women but not men *Pike et al, 2011, Neuropsychologica*
AIBL: women and AD

- Complete assessment of 200 women from the Women’s Healthy Ageing Cohort
- Longitudinal, Prospective data from midlife 20 years prior to disease.
- Cohort cognition previously assessed in 2002 and 2004
- Reassessed in 2011/12 and 2013/14 (65-75yoa) with MRI and Amyloid imaging in all.
### AIBL: women and AD

#### Midlife
- **AIBL**
- **eMCI**
- **HC**
- **IMCI**

#### Post Menopausal
- **ADNI I**
- **ADNI II**
- **ADNI GO**

<table>
<thead>
<tr>
<th>Baseline Midlife</th>
<th>1st Cognitive Assessments Post Menopausal</th>
<th>aiblWHAP to commence Ageing</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age 45-55</td>
<td>Age 55-65</td>
<td>Age 65-75</td>
</tr>
<tr>
<td>Annual Follow-up over 8 years</td>
<td>2 assessments 2 years apart</td>
<td>2 assessments 18 months apart MRI &amp; Amyloid Scans</td>
</tr>
</tbody>
</table>
AIBL: ongoing

• “AIBL Active” – exercise intervention in 150 HC/MCI study
• Funded by NHMRC
• Commenced Intervention
• PET and MRI in all participants
AIBL Study Team

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Research and Standardisation in Alzheimer’s Disease

RASAD

Melbourne, Australia, 27-29 March, 2012
Thank you

Contact Us

www.aibl.csiro.au